Appl. No.: 10/599,448 Amdt. dated August 10, 2009

Reply to Office Action of February 13, 2009

## Amendments to the Claims:

## 1-34. (Cancelled)

- 35. (Currently Amended) An HIV <u>immunogenic vaccine</u> composition characterized in that it comprises at least one <u>isolated Tat antigen which is a stabilized</u> Tat antigen resistant to proteolytic degradation, said stabilized antigen being selected from the group consisting of:
- a) a complex Tat/ligand comprising at least an HIV Tat protein or a Tat fragment of at least 11 amino acids, and a non-metal ligand of Tat,
- b) an artificial variant of an HIV Tat protein or of a Tat fragment of at least 11 amino acids, wherein one to seven cysteines located at positions 22, 25, 27, 30, 31, 34 and/or 37 of the Tat amino acid sequence are modified with a hydrophobic group and/or substituted with a hydrophobic amino acid chosen from: Leucine, Isoleucine, Methionine, Phenylalanine, Tryptophan, Tyrosine and the hydrophobic analogs of said amino acids, and
- c) a complex between the artificial variant of a Tat protein or of a Tat fragment defined in b), and a non-metal ligand of Tat.
- 36. (Currently Amended) The <u>immunogenic vaccine</u> composition as claimed in claim 35, characterized in that said non-metal ligand in a) or in c) is protein, lipid, carbohydrate, nucleotide, <u>glycolipid or glycoprotein or mixed in nature</u>.
- 37. (Currently Amended) The <u>immunogenic vaccine</u> composition as claimed in claim 36, characterized in that said non-metal ligand in a) or in c) is a polysulfated sugar chosen from: dextran sulfate, pentosan polysulfate and polysulfated glycosaminoglycans, including heparin or heparan sulfate.

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- 38. (Currently Amended) The <u>immunogenic vaccine</u> composition as claimed in claim 37, characterized in that said heparin is a heparin having a molecular weight of 15000 Da or a heparin fragment having a molecular weight of 6000 Da.
- 39. (Currently Amended) The <u>immunogenic vaccine</u> composition as claimed in claim 36, characterized in that said non-metal ligand in a) or in c) is the HIV Vpr protein.
- 40. (Currently Amended) The <u>immunogenic vaccine</u> composition as claimed in claim 35, characterized in that at least the four cysteines at positions 25, 27, 30 and 31 are substituted with a hydrophobic amino acid and/or modified with a hydrophobic group.
- 41. (Currently Amended) The <u>immunogenic vaccine</u> composition as claimed in claim 35, characterized in that said hydrophobic amino acid is selected from the group consisting of: a leucine, a tryptophan and a phenylalanine and/or said hydrophobic group is S-tert-butyl.
- 42. (Currently Amended) The <u>immunogenic vaccine</u> composition as claimed in claim 35, characterized in that said stabilized Tat antigen derives from an inactivated Tat protein or from an inactivated Tat fragment.
- 43. (Currently Amended) The <u>immunogenic vaccine</u> composition as claimed in claim 42, characterized in that said inactivated Tat protein or said inactivated Tat fragment comprises the substitution of each of the cysteines at positions 22, 34 and 37 to serines or else the substitution of each of the arginines at positions 52 and 53 to glutamines.
- 44. (Currently Amended) The <u>immunogenic</u> vaccine composition as claimed in claim 35, characterized in that said Tat protein or the fragment of said protein is

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chosen from: the Tat protein of 101 amino acids, the Tat protein of 86 amino acids, the fragment 1 to 57 of Tat and the fragments of at least 11 amino acids included in <u>said Tat</u> the proteins of 101 or 86 amino acids or <u>said</u> fragment 1 to 57 of Tat above.

- 45. (Currently Amended) The <u>immunogenic vaccine</u> composition as claimed in claim 35, characterized in that said <u>HIV Tat proten in a) or b) comprises stabilized Tat antigen derives from the Tat protein of the sequence SEQ ID NO: 1 or from a fragment of at least 11 amino acids of this sequence.</u>
- 46. (Currently Amended) The <u>immunogenic vaccine</u> composition as claimed in claim 35, characterized in that said Tat protein or said Tat fragment in a) is also complexed with a metal ion chosen from polyvalent cations, preferably divalent cations, such as Zn<sup>2+</sup> or Cd<sup>2+</sup>.
- 47. (Currently Amended) The <u>immunogenic vaccine</u> composition as claimed in claim 35, characterized in that said artificial variant of a Tat protein or of a Tat fragment in b) or in c) is also complexed with a metal ion-chosen from polyvalent eations, preferably divalent cations, such as Zn<sup>2+</sup> or Cd<sup>2+</sup>.
- 48. (Currently Amended) The <u>immunogenic</u> vaccine composition as claimed in claim 35, characterized in that said Tat protein or said Tat fragment is a monomer.
- 49. (Currently Amended) The <u>immunogenic vaccine</u> composition as claimed in claim 35, characterized in that said Tat protein or said Tat fragment is an oligomer, preferably a dimer.
- 50. (Currently Amended) The <u>immunogenic vaccine</u> composition as claimed in claim 49, characterized in that said oligomer, preferably dimer, is formed from the covalent association of said Tat protein and/or of the fragment of said protein by means

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of an intermolecular disulfide bond involving one of the cysteines at position 22, 25, 27, 30, 31, 34 or 37.

- 51. (Currently Amended) The <u>immunogenic vaccine</u> composition as claimed in claim 50, characterized in that said disulfide bond involves one of the cysteines at position 22, 34 or 37.
- 52. (Currently Amended) The <u>immunogenic vaccine</u> composition as claimed in claim 51, characterized in that the Tat dimer is formed from the association, by means of a disulfide bridge between the cysteines at position 34, of two Tat proteins or of two Tat fragments of at least 11 amino acids comprising a serine at positions 22 and 37 and a leucine at positions 25, 27, 30 and 31.
- 53. (Currently Amended) The <u>immunogenic vaccine</u> composition as claimed in claim 49, characterized in that said oligomer, preferably dimer, is formed from the noncovalent association of said Tat protein and/or of the fragment of said protein by means of metal ions, preferably of polyvalent cations, in particular divalent cations such as  $Zn^{2+}$  and  $Cd^{2+}$ .
  - 54. (Cancelled).
- 55. (Currently Amended) The <u>immunogenic</u> vaccine composition as claimed in claim 35, characterized in that it comprises a pharmaceutically acceptable vehicle and/or an adjuvant and/or a carrier substance.
- 56. (Currently Amended) The <u>immunogenic vaccine</u> composition as claimed in claim 55, characterized in that it consists of said stabilized antigen and a pharmaceutically acceptable vehicle and/or a carrier substance.

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57. (Currently Amended) The <u>immunogenic</u> vaccine composition as claimed in claim 55, characterized in that said adjuvant is alumina hydroxide.

## 58. - 66. (Cancelled).

- 67. (New) The immunogenic composition as claimed in claim 46, characterized in that said metal ion is a polyvalent cation.
- 68. (New) The immunogenic composition as claimed in claim 46, characterized in that said metal ion is a divalent cation.
- 69. (New) The immunogenic composition as claimed in claim 46, characterized in that said metal ion is  $Zn^{2+}$  or  $Cd^{2+}$ .
- 70. (New) The immunogenic composition as claimed in claim 47, characterized in that said metal ion is a polyvalent cation.
- 71. (New) The immunogenic composition as claimed in claim 47, characterized in that said metal ion is a divalent cation.
- 72. (New) The immunogenic composition as claimed in claim 47, characterized in that said metal ion is  $Zn^{2+}$  or  $Cd^{2+}$ .
- 73. (New) The immunogenic composition as claimed in claim 49, characterized in that said oligomer is a dimer.
- 74. (New) The immunogenic composition as claimed in claim 50, characterized in that said oligomer is a dimer.

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- 75. (New) The immunogenic composition as claimed in claim 53, characterized in that said oligomer is a dimer.
- 76. (New) The immunogenic composition as claimed in claim 53, characterized in that said metal ions are polyvalent cations.
- 77. (New) The immunogenic composition as claimed in claim 53, characterized in that said metal ions are divalent cations.
- 78. (New) The immunogenic composition as claimed in claim 53, characterized in that said metal ions are  $Zn^{2+}$  or  $Cd^{2+}$  ions.
- 79. (New) An HIV immunogenic composition, characterized in that it comprises at least one polynucleotide or one recombinant vector encoding:
- a) an HIV Tat protein or a Tat fragment of at least 11 amino acids, and a peptide ligand of Tat,
- b) an artificial variant of an HIV Tat protein or of a Tat fragment of at least 11 amino acids, wherein one to seven cysteines located at positions 22, 25, 27, 30, 31, 34 and/or 37 of the Tat amino acid sequence are substituted with a hydrophobic amino acid chosen from: Leucine, Isoleucine, Methionine, Phenylalanine, Tryptophan, Tyrosine and the hydrophobic analogs of said amino acids, and
- c) a complex between the artificial variant of a Tat protein or of a Tat fragment defined in b), and a peptide ligand of Tat.